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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/461,684 | 12/14/99 | LAUS | R 7636-0020.30 |

| EXAMINER | |
|---|---|
| DIBRINO, M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | 9 |

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HM12/0730

**DATE MAILED:** 07/30/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

1- File Copy

PTO-90C (Rev. 2/95)

*U.S. GPO: 2000-473-000/44602

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/461,684 | Laus et al. |
| **Examiner** | **Art Unit** |
| Marianne DiBrino | 1644 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on Jul 2, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 1-7 is/are pending in the applica

4a) Of the above, claim(s) 3 is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1, 2, and 4-7 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

**Application Papers**

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4&5 Filed 4/10/00 & 6/19/00, respectively

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☒ Other: *Notice to Comply with the Sequence Rules*

## DETAILED ACTION

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

2. Applicant is required under 37 C.F.R. 1.821(d) to amend the specification to list the appropriate SEQ ID NOS for sequences disclosed in the specification (for example, page 3 in the Brief Description of the Drawings for Figure 3, page 7 at lines 33-35, page 8 at lines 8-9, Table 1 at the last two entries, page 14 at line 41, page 17 at lines 15 and 17 and claim 3 at lines 4-6).

3. Applicant's response filed 7/2/01 (Paper No. 8) is acknowledged and has been entered.

Claims 1-7 are pending.

4. Applicant's election of Group I (claims 1-7) without traverse, and species of SEQ ID NO: 6 with traverse in Paper No. 16 is acknowledged.

As the basis for traversal of the species restriction requirement, Applicant cites MPEP 803.04, i.e., that "It has been determined that normally ten" [nucleotide] sequences constitute a reasonable number for examination purposes. It is the Examiner's position that the instant claims are drawn to a composition comprising a peptide, not a nucleotide.

**The requirement is still deemed proper and is therefore made FINAL.**

Claims 1, 2 and 4-7 read on the elected species, SEQ ID NO: 6.

Accordingly, claim 3 (non-elected species of Group I)is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1, 2 and 4-7 are currently being examined to the extend they read upon the elected species SEQ ID NO: 6.

5. The disclosure is objected to because of the following informalities:

a. The Brief Description of the Drawings discloses "Fig. 6A and Fig. 6B" at line 6 on page 4. There are no Fig. 6A and Fig. 6B.

b. It is noted that this application appears to claim subject matter disclosed in Provisional application serial no. 60/112,234, filed 12/14/1998. Although reference to the prior application was inserted as the first sentence of the specification of this application, it is noted that the filing date was not disclosed. The first sentence of the specification should refer to the provisional application using language such as:
This application claims the benefit of U.S. Provisional Application No. 60/____, filed ____.

c. There is a spelling error in claim 5 at line 2; "anitgen" should be "antigen".

Applicant is reminded with respect to "a" that amendments must not introduce new matter.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Applicant is reminded of the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999; the following rejection is set forth herein.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of the claimed antigen composition comprising an "added peptidic sequence" which facilitates entry of said antigen into antigen presenting cells (APC).

The instant claims encompass a composition comprising an antigen with an added peptidic sequence which has the property of facilitating the entry of the antigen into APC and is capable of eliciting an enhanced CTL response in the context of MHC class I. There is insufficient disclosure in the specification on such a composition.

The specification discloses, in the paragraph spanning pages 5 and 6, that CTL are induced when a protein enters the MHC class I pathway of cytosolic antigen

processing in an APC. The specification further discloses, in the paragraph spanning pages 6 and 7, that the typical response to soluble protein antigens is a Class II [MHC] mediated response, and that the compositions of the present invention allow soluble protein antigens to enter the Class I pathway which is typically reserved for foreign cellular antigens. The specification further discloses that peptidic sequences such as those represented by one or more of SEQ ID NO: 1-7 or those disclosed on page 7 at lines 29-36 are linked to an antigen, the antigen is capable of triggering naive CTL responses in vivo, and is more efficient in stimulating corresponding Class I restricted memory T cells in vitro (page 7 at lines 19-36).

In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. However, a generic statement such as "added peptidic sequence" without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by the property of facilitating entry of the antigen into APC. It does not specifically define any of the "added peptidic sequence[s]". It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by the said property of facilitating entry of an antigen into an APC does not suffice to define the genus because it is only an indication of what the property the "added peptidic sequence" has. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many such species may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

The instant disclosure of a few species or subgenera of "added peptidic sequence" does not adequately describe the scope of the claimed genus. Structural features that distinguish members of the genus from others excluded are missing from the disclosure. Because of this lack of disclosure of sufficient relevant identifying characteristics and because the genus is highly variant, the disclosure is insufficient to describe the genus.

8. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for making and/or using a composition comprising an antigen and an added peptidic sequence which facilitates entry of an antigen into APC that comprises one or more of SEQ ID NO: 1-7 or those disclosed on page 7 at lines 29-36 for the purpose of eliciting an enhanced CTL response, does not reasonably provide enablement for making and/or using a composition comprising an added peptidic sequence that is not one or more of SEQ ID NO: 1-7 or the sequences disclosed on page 7 at lines 29-36. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification does not disclose how to make and/or use the instant invention wherein the added peptidic sequence that is not one or more of SEQ ID NO: 1-7 or the sequences disclosed on page 7 at lines 29-36. The claimed composition comprises any added peptidic sequence with the property of facilitating entry of an antigen into APC. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass a composition comprising added peptidic sequences which are not not one or more of SEQ ID NO: 1-7 or the sequences disclosed on page 7 at lines 29-36. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed composition can be made and/or used. The specification discloses no working examples that are not comprised of SEQ ID NO: 1 and SEQ ID NO: 2.

The specification discloses, in the paragraph spanning pages 5 and 6, that CTL are induced when a protein enters the MHC class I pathway of cytosolic antigen processing in an APC. The specification further discloses, in the paragraph spanning pages 6 and 7, that the typical response to soluble protein antigens is a Class II [MHC] mediated response, and that the compositions of the present invention allow soluble protein antigens to enter the Class I pathway which is typically reserved for foreign cellular antigens. The specification further discloses that peptidic sequences such as those represented by one or more of SEQ ID NO: 1-7 or those disclosed on page 7 at lines 29-36 are linked to an antigen, the antigen is capable of triggering naive CTL responses in vivo, and is more efficient in stimulating corresponding Class I restricted memory T cells in vitro (page 7 at lines 19-36).

Evidentiary references Osicka et al (Inf. Immun. 86/1: 247-256, 2000, Abstract) and Guermonprez et al (J. Immunol. 162/4: 1910-1916, 1999, Abstract) teach OVA antigen with added peptidic sequence from ACT-Hly which delivers the antigen into the MHC class I antigen processing pathway.

In view of the lack of predictability of the art to which the invention pertains, undue experimentation would be required to make and/or use "added peptidic sequences" which are not one or more of SEQ ID NO: 1-7 or one of the sequences disclosed on page 7 at lines 29-36 of the instant specification. The enablement provided by the specification is not commensurate with the scope of the claims.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1, 2 and 4-7 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Buschle et al (PNAS USA 94: 3256-3261, 4/1997, IDS reference) in view of Kim et al (J. Immunol. 159(4): 1666-1668, 8/1997).

Buschle et al teach that polycationic amino acids have been employed to enhance transport of proteins into cells and teach the ability of different cationic polymers, two of which are poly-Arg and poly-Lys, to transfer peptides to APCs (especially Abstract). Buschle et al teach compositions comprising antigenic peptides from pathogens and tumors and poly-Lys or poly-Arg (especially Abstract, Table 1 and page 3258, column 2 first full paragraph).

Buschle et al do not teach a composition comprising an antigen having an added peptidic sequence, wherein the added peptidic sequence is linked to the said antigen, nor wherein the antigen-polycationic sequence is a fusion protein.

Kim et al teach that because exogenous proteins do not ordinarily enter the cytosol [of APC] and access the MHC class I-processing pathway, protein-based vaccines that induce class I-restricted CTL responses have proved difficult to design. Kim et al further teach that they

have addressed this problem by conjugating OVA antigen to a cationic peptide derived from HIV-1 tat which has a cysteine at the carboxy terminal end, and teach administration of a composition comprising the antigen/cationic peptide to APC leads to processing and presentation of the peptides in association with Class I MHC (especially Abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made an N-terminal cysteinylated peptide (as taught by Kim et al) version of the cationic poly-Lys or the poly-Arg peptide taught by Buschle et al to have conjugated it to one of the antigens taught by Buschle et al or Kim et al as taught by Kim et al for the antigen/cationic peptide of Kim et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to do this to enhance the transport of proteins or peptides from pathogens or tumors into the class I processing pathway and to stimulate CTL responses because Kim et al teach that protein-based vaccines that induce class I-restricted CTL responses have proved difficult to design and conjugation of an antigen to a cationic peptide leads to class I MHC processing and presentation, Buschle et al teach that polycationic amino acids have been employed to enhance transport of proteins into cells, they teach the ability of different cationic polymers, two of which are poly-Arg and poly-Lys, to transfer peptides to APCs and they teach compositions comprising antigenic peptides from pathogens or tumors and poly-Lys or poly-Arg. The instant claims 2 and 4-7 are included in this rejection because SEQ ID NO: 6 is poly-Arg or poly-Lys, and it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used any length poly-Lys or poly-Arg that was effective. Claim 6 is included in this rejection because claimed recitation of intended use in immunizing a subject against a tumor or pathogen wherein the antigen is specific to the tumor or antigen does not carry any patentable weight per se. A compound is the same compound irrespective of its intended use. Claim 7 is included in this rejection because the recitation of a method wherein the claimed product is made carries no patentable weight in this product claim.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
July 23, 2001

CHRISTINA Y. CHAN
SUPERVISORY PATENT EXAMINER
GROUP ~~1800~~ 1640

Application No.: 09/461,684

# NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

[X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

[ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

[ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

[ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

[ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

[ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

[X] 7. Other: Applicant is required to provide SEQ ID NOS for all sequences disclosed in the specification (for example, page 3 in the Brief Description of the Drawings for Figure 3, page 7 at lines 33-35, page 8 at lines 8-9, Table 1 at the last two entries, page 14 at line 41, page 17 at lines 15 and 17 and claim 3 at lines 4-6).

**Applicant Must Provide:**

[X] An ~~initial or~~ substitute computer readable form (CRF) copy of the "Sequence Listing".

[X] An ~~initial or~~ substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

[X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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